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09/369,992	08/06/1999	ANNA KATE URSULA KARA	64-99	7524

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/369,992	Applicant(s) Kara et al
	Examiner Portner	Art Unit 1645

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 16, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 5-11, 13-15, and 46* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 5-11, 13-15, and 46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 2-4, 12, 16-45 have been canceled.

Claims 1, 5, 8-10, 13 have been amended; new claim 46 has been added.

Claims 1, 5-11, 13-15 and 46 are pending and under consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

2. Claims 1-2 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, in light of the cancellation of claim 2 and the amendment of claim 1 to recite the claim limitations of claim 4.

3. Claim 1 rejected under 35 U.S.C. 112, second paragraph for reciting claim limitations that did not distinctly claim the invention relative to the sample being any biological sample, is obviated in light of Applicant's clarifying narrative.

4. Claims 2-4 rejected under 35 U.S.C. 112, second paragraph, in light of the cancellation of these claims.

5. Claim 8 rejected under 35 U.S.C. 112, second paragraph for not positively reciting a signal producing means, has been obviated in light of the amendment of claim 8 to positively recite the presence of an identifiable signal.

6. Claim 9, rejected under 35 U.S.C. 112, second paragraph, in light of the claim no longer reciting the phrase "such as".

7. Claim 10 rejected under 35 U.S.C. 112, second paragraph for broadening the scope of claim 1 by defining the primers or primer pairs to be Plasmodium genus specific, in light of the claim having been amended to no longer recite the phrase "genus specific".

8. Claim 11 rejected under 35 U.S.C. 112, second paragraph, in light of the amendment of claim 1 to recite an RNA detection means.

9. Claim 13 rejected under 35 U.S.C. 112, second paragraph in light of the amendment of claim 13 to recite the "selected from the group consisting of".

10. Claims 1-2, 5-7, 8-10, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ayyanathan et al (1996), in light of the amendment of claim 1 to recite the species of claim 4, and cancellation of claim 2.

11. Claims 1, 5-8, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by McCutchan et al (US Pat. 4,707,445), in light of the amendment of claim 1 to recite the species of claim 4.
12. Claims 1, 5-9, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by McCutchan et al, (Science, 1984), in light of the amendment of claim 1 to recite the species of claim 4.
13. Claims 1, 5-6 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by McCutchan et al, (1988, Molecular and Biochemical parasitology), in light of the amendment of claim 1 to recite the species of claim 4.
14. Claims 1, 5-9, 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Das et al, (Analytical Biochemistry, 1996), in light of the amendment of claim 1 to recite the species of claim 4.
15. Claim 1, 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gardner et al (1994), in light of the amendment of claim 1 to recite the species of claim 4.
16. Claims 1-3, 5-10, 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Obst et al, (1990, Histochemistry), in light of the amendment of claim 1 to recite the species of claim 4.

Rejections Maintained

17. (Amended and new claim) Claims 1, 5-11, 13-15 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description.*
18. (Amended) Claims 1, and 5-11, 13-15, 46 are rejected under 35 U.S.C. 112, second paragraph which define the probe or primer to comprise one or two components, the first being one that is a sequence of the extrachromosomal element of P.berghei or is a " nucleic acid derived therefrom" which refers back to: the "sample" , the Plasmodium berghei probe or primer, the Plasmodium berghei extrachromosomal genetic element and Plasmodium berghei. This phrase does not clearly define what the derived "nucleic acid" is as the source of the sample is not defined, the extrachromosomal element is not defined to be a plastid and may be any nucleic acid that is not chromosomally associated, the manner in which the nucleic acid is derived is not distinctly claimed, and the probe or primer is conserved in a malarial agent of humans, which is not Plasmodium berghei which infects rodents (rats and mice).

19. (elected species/amended) Claims 1,5-9, 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Gardner et al (1993, Nucleic acid research), for reasons of record in paper number 29, paragraph 18.

Response to Arguments

20. The rejection of claims 1, 5-11, 13-15 and 46 under 35 U.S.C. 112, first paragraph (*written description)*, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is traversed on the grounds that:

a. Example 6 provides original descriptive support for the instantly amended invention, wherein a primer set of SEQ ID NO 5 and 6 were used to determine the P.berghei extra chromosomal genetic element is transcriptionally active; Example 7 shows the assay of blood samples in the presence of a "Plasmodium spp." ;

b. Tables 3-4 show that primer sets using SEQ ID NO 5 and 6 are capable of detecting P.falciparum, P.vivax, P.ovale and Pl.malariae in 100% of the cases;

c. Table 5 shows LSU-rRNA similarity between four species of Plasmodium (falciparum, vivax, ovale and malariae, the species compared do not include P.berghei; and

d. Concludes that smaller sequences of nucleotides 1147-1740 would be effective to detect malarial species.

21. It is the position of the examiner that:

a. the instantly claimed invention does not recite the SEQ ID NO 5 and 6 primer set used to traverse the instant rejection;(none of the claims recite this primer set)

b.the probe or primer is not required to detect 100% of the malarial parasites all of the time as argued by Applicant;

c.the claims recite a genus of probes and primers which may be:

i. a nucleic acid derived from(a sequence that comprises a portion of nucleotides 1147-1740 of SEQ Id NO 1) "the sample", "the extrachromosomal genetic element" or a nucleic acid derived from a probe or primer of nucleotides 1147-1740 of SEQ Id No 1.

Applicant's arguments are not commensurate in scope with the instantly claimed invention, which has not described the genus of probes and primers derived from "the sample, the probe, primer or the extra chromosomal genetic element, or a probe or primer that only comprises a portion of the nucleotide sequence set forth in nucleotides 1147-1740 of SEQ ID NO 1.

Reference sequence SEQ ID No 1: 1147-1740 ---------- NA

Claimed probe or primer used in method: ??????????????????-------???????????????

The lack of written description over the combination of claim limitations directed to "a nucleic acid derived therefrom" and "comprises a sequence that is highly conserved" is maintained for reasons of record.

Amendment of claim 1 to recite nucleotides 1147 to 1740, or a portion consisting of 15 consecutive nucleotides or more of the nucleotides set forth in SEQ ID NO 1 would be a combination of claim limitations which evidences original descriptive support in the instant specification and would be commensurate in scope with Applicants arguments; this combination of claim limitations could obviate this rejection.

22. The rejection of claims 1, and 5-11, 13-15, 46 under 35 U.S.C. 112, second paragraph for reciting claim limitations that define the probe or primer to be a " nucleic acid derived therefrom", a phrase referring back to: the "sample" , the Plasmodium berghei probe or primer, the Plasmodium berghei extrachromosomal genetic element and Plasmodium berghei, is traversed on the grounds that:

a. "In view of the amendment of claim 1 to recite a particular sequence embodied in the probe or primer",

b.the cancellation of various claims and amendment of others, the rejection of claims 2-11, and 13-15 for reciting the phrase a " nucleic acid derived therefrom" has been obviated.

23. It is the position of the examiner that how or what the derived sequence is, has not been clarified in light of the fact that the probe or primer need only comprise a fragment of the recited nucleotide sequence and the size or portion of nucleotides 1147 to 1740 of SEQ ID NO 1, is not required to be 15 consecutive nucleotides of the recited range, but must only be 15 nucleotides in length and hybridize to any plasmodium malarial agent in a biological sample, the biological sample not being limited to a biological sample from any specific source.

a.Additionally, the phrase "a nucleic acid derived therefrom" does not clearly define what the derived "nucleic acid" is as the source of the sample is not defined, the extrachromosomal element is not defined to be a plastid and may be any nucleic acid that is not chromosomally associated, the manner in which the nucleic acid is derived is not distinctly claimed, and the probe

or primer is conserved in a malarial agent of humans, which is not Plasmodium berghei which infects rodents (rats and mice).

Applicant arguments are not commensurate in scope with the instantly claimed invention.

24. The rejection of claims 1,5-9, 10-14 under 35 U.S.C. 102(b) as being anticipated by Gardner et al (1993, Nucleic acid research), is traversed on the grounds that "This reference does not teach or suggest the sequence of the probe or primer recited in amended claim 1".

25. It is the position of the examiner that the probe or primer of claim 1 must only comprise a portion (gene fragment) of nucleotides 1147 to 1740 of SEQ ID NO 1, and is not so limited to only the utilization of nucleotides 1147 to 1740 of SEQ ID NO 1 as the probe or primer, nor are the claims limited to the primer pair combination of SEQ ID NO 5 or 6, which Applicant has used to traverse other rejections of the claims, but the claimed invention is directed to any nucleic acid derived from the recited range of nucleotides and is capable of detecting a malarial agent in a biological sample. Applicant's arguments are not commensurate in scope with the instantly claimed invention.

The biological sample of Gardner was a parasitized erythrocyte sample (see page 1068, col. 1, Transcript analysis, paragraph 5).

The probe or primer was derived from the LSU rRNA (see page 1068, col. 1, paragraph 5 "an oligonucleotide complementary to sequence near the 5' end of the LSU rRNA" and " The

complete DNA sequence of the LSU gene is deposited in the EMBL database under the accession number X61660", col. 1, paragraph 4).

The detection was by RNA PCR (see page 1068, col. 1, paragraphs 3-5); specific portions of the LSU rRNA genes were made (see Table 1, page 1070, col.1-2, especially, col. 1, first three lines define the most conserved positions and Table 1, col. 2; Figure 4) that comprises a LSU rRNA nucleic acid sequence of SEQ ID NO 1, nucleotides 1147-1740 that is conserved (complementary to "A/U", see page 1068, col. 1, paragraph 3) and found in an extrachromosomal element circular DNA that is a plastid (see sequence alignment) of a human malarial agent, wherein the probe or primer hybridized to DNA from a human malarial agent in the sample (see Figure 4, page 1070); to permit detecting hybridization (see page 1070, figure 4), wherein the probe was at least 15 nucleotides in length (see page 1067, materials and methods, DNA analysis section and sequence alignment for X61660 and Figure 4, image and narrative).

The hybridization conditions for RNA analysis were disclosed in light of references 7 & 8 (see page 1067, col. 2, paragraph 2, lines 1-2; Gardner et al 1991, Molecular and Biochemical Parasitology, Vol. 48, (reference of record) define a plurality of hybridization conditions, see page 78, col. 2, paragraphs 2-3 and col. 1-2 of page 79, the conditions being low, medium and high stringency conditions). The rejection is maintained for reasons of record in paper number 29, paragraph 18. Amendment of the claims to be commensurate in scope with the arguments set forth by Applicant could obviate this rejection; specifically limiting the claim to only a probe or primer that comprises nucleotides 1147 to 1740 of SEQ ID No 1.

New Claim/New Combination of Claim Limitations/New Grounds of Rejection
Claim Rejections - 35 U.S.C. § 103

26. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

27. Claims 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gardner et al (1993, Nucleic acid research, reference of record) in view of Obst et al, (1990, Histochemistry, reference of record).

Gardner et al teach and show a method of detecting a human Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a blood derived (erythrocyte) biological sample with a probe or primer (see DNA analysis section, page 1067, col. 2; page 1070, col. 1, first three lines define the most conserved positions and Table 1, col. 2; Figure 4) that comprises a LSU rRNA nucleic acid sequence of SEQ ID NO 1, nucleotides 1147-1740 that is conserved (complementary to "A/U", see page 1068, col. 1, paragraph 3) and found in an extrachromosomal element circular DNA that is a plastid (see sequence alignment) of a human malarial agent, wherein the probe or primer hybridized to DNA from a human malarial agent in the sample (see Figure 4, page 1070); to permit

detecting hybridization (see page 1070, figure 4), wherein the probe was at least 15 nucleotides in length (see page 1067, materials and methods, DNA analysis section and sequence alignment for X61660 and Figure 4, image and narrative).

Gardner et al (page 1068, col. 1, paragraph 3, middle of paragraph), teaches a highly conserved sequence of P.falciparum, the complement thereof was incorporated into a primer for detecting a Plasmodial malarial agent of human in a biological sample and the primer comprised a highly conserved sequence for P.berghei (see sequence alignment of X61660), and utilized a detectable signal for the detecting of hybridization but differs from the instantly claimed invention by failing to show the signal to be generated by a non-isotopic reporter molecule biotin, and the biological sample to be a dried blood sample.

Obst et al teach a method of detecting a Plasmodium malarial agent in a biological sample, the method comprising the steps of: contacting and detecting hybridization in a dried blood sample (see page 101, col. 2, material and methods, paragraph 2) which utilized a biotin reporter molecule (see page 102, col. 2, paragraph 3; page 103, col. 1-2 Discussion section and all frames of Figure 1) in an analogous art for the purpose of detecting a malarial agent utilizing a non-isotopic reporter molecule which generates a specific signal with high resolution (see page 102, col. 2, paragraph 2, last three lines).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of Gardner et al to include the analysis of dried blood samples and a biotin non-isotopic signal reporter molecule as suggested and taught by Obst et al

because both Gardner et al and Obst et al teach methods of detecting a malarial agent in a blood derived biological sample, and Obst et al teaches that dried blood smears are readily used as a biological sample for the detection of a malarial agent, and Obst et al also teaches the advantage of utilizing a biotin non-isotopic reporter molecule for the attainment of enhanced signal generation (see page 102, col. 2, hybridization signal as a function of the probe).

In the absence of a showing of unexpected results, the person of ordinary skill in the art would have been motivated by the reasonable expectation of detecting a malarial agent in a dried blood sample utilizing an LSU rRNA biotin report molecule utilizing the probe or primer of Gardner et al with the biotin reporter molecule of Obst et al because Obst et al teach a non-isotopic reporter molecule biotin defined and provided means for generating a specific signal with high resolution (see page 102, col. 1, paragraph 3, signal detection and col. 2, paragraph 2, last three lines) due do the ability of biotin to specifically interact with a fluorescently labeled anti-biotin antibody system which resulted in a highly amplified the biotin signal reporter molecule of high resolution. Gardner et al in view of Obst et al obviates the instantly claimed invention.

Conclusion

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp August 4, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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